Exhibit 1d

FEDERAL BUREAU OF PRISONS
CLINICAL PRACTICE GUIDELINES FOR THE PREVENTION AND TREATMENT OF VIRAL HEPATITIS
February 2003

PURPOSE

The Federal Bureau of Prisons Clinical Practice Guidelines for the Prevention and Treatment of Viral Hepatitis provide recommendations for the medical management of Federal inmates who have viral hepatitis or who are otherwise at risk of infection.

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DEFINITIONS

GENERAL DEFINITIONS

Clinician is a physician or mid-level provider.

Absolute contraindication is a condition or factor that in and of itself ordinarily precludes a specific intervention.

Relative contraindication is a condition or factor that may preclude a specific intervention when considered in conjunction with other criteria.

Qualitative viral assay is a nucleic acid test (NAT) used to detect the presence, but not the amount of virus present.

Quantitative viral assay is a nucleic acid test (NAT) used to measure the amount of virus present.

Standard precautions are protective measures used for all patient/inmate contacts and situations to prevent the spread of infections transmitted by contaminated blood and body fluids. Precautions include the wearing of gloves and other personal protective equipment (personal protective equipment should be an impervious barrier) when soiling is likely; and procedures for protective handling (handling includes the use of puncture-resistant devices and leak-proof protection) of contaminated materials and equipment, and routine cleaning of all contaminated surfaces and equipment.

HEPATITIS A

Hepatitis A is an acute viral hepatitis caused by a highly infectious RNA virus that is transmitted primarily by the fecal-oral route and close personal contact. Acute hepatitis A has a mild to fulminant clinical presentation that resolves without progression to chronic infection or chronic hepatitis.

HAV is hepatitis A virus, an enveloped RNA virus.

IgM anti-HAV is the antibody subclass to HAV that develops with acute infection.

IgG anti-HAV are antibodies to HAV that confer immunity.

Total anti-HAV are total antibodies to HAV that include IgG and

IgM antibody subclasses.

HEPATITIS B

Hepatitis B is an acute or chronic viral hepatitis caused by a DNA virus that is transmitted primarily through sexual contact, exposures to blood, and perinatally.

HBV is hepatitis B virus, a double-stranded DNA virus.

HBsAg is hepatitis B surface antigen, a viral envelope antigen that is detectable during acute or chronic HBV infection.

HBeAg is hepatitis e antigen, a secreted, viral antigen of the hepatitis B viral core that is indicative of active viral replication and increased infectiousness.

Anti-HBs is the antibody to hepatitis B surface antigen that confers immunity to HBV infection. Anti-HBs is usually detectable after infection with HBV and following vaccination.

IgM anti-HBc is the antibody to hepatitis B core antigen that develops with acute HBV infection.

Total anti-HBc is the total antibody response to hepatitis B core antigen that is detectable after acute HBV infection and remains detectable during convalescence. Measurement of total anti-HBc is a useful screen for past HBV infection. Total anti-HBc is not detectable following hepatitis B vaccination.

Anti-HBe is the antibody to hepatitis e antigen that develops as viral replication and active hepatitis B begin to wane. Development of anti-HBe coincides with the loss of HBe antigen.

HEPATITIS C

Hepatitis C is an acute or chronic viral hepatitis caused by an RNA virus that is transmitted primarily by percutaneous contact with blood.

HCV is hepatitis C virus, an enveloped, single-stranded RNA virus.

Anti-HCV is the antibody to HCV core and nonstructural proteins that is detectable from several weeks to months after clinical

hepatitis.

Anti-HCV screening assay is an immunoassay such as an enzyme immunoassay (EIA) or chemiluminescence immunoassay (CIA) used to screen for HCV infection by measuring antibodies to HCV antigens. The detection of anti-HCV by immunoassay with a high signal-to-cutoff ratio, or in a person with risk factors for HCV infection, is highly predictive of HCV infection.

RIBA (anti-HCV) is the recombinant immunoblot assay that measures antibodies to HCV antigens through immunoblot technology. Measurement of anti-HCV by RIBA is used as a supplementary, "confirmatory" test for HCV infection for persons without risk factors for HCV infection who have detectable anti-HCV by a screening immunoassay; OR for persons with or without risk factors for HCV infection who have detectable anti-HCV by a screening immunoassay with a low signal-to-cutoff ratio.

Anti-HCV indeterminant is a positive anti-HCV screening immunoassay with a supplemental RIBA test that is inconclusive.

Early viral response (EVR) after treatment of chronic hepatitis C with pegylated interferon and ribavirin is a minimum two log decrease in the level of HCV RNA after the first 12 weeks of treatment compared to pretreatment levels, as measured by a quantitative nucleic acid test (NAT).

Sustained viral response (SVR) after antiviral treatment of chronic hepatitis C is the absence of detectable HCV RNA in the serum 24 weeks after treatment is completed, measured by a qualitative NAT for HCV RNA with a lower limit of detection of 50 IU/ml or less.

HEPATITIS D

HDV is hepatitis delta virus, a defective single-stranded RNA virus that requires HBV for structural integrity and replication.

Hepatitis D or delta hepatitis is an acute or chronic hepatitis caused by HDV.

HBV-HDV coinfection is the simultaneous infection of HBV and HDV.

HBV-HDV superinfection is acute HDV infection in a person with preexisting chronic HBV infection (HBsAg-positive).

HDAg is hepatitis delta antigen.

IgM anti-HDV is an antibody subclass to HDV.

IgG anti-HDV is an antibody subclass to HDV.

CIRRHOSIS

Compensated cirrhosis is cirrhosis of the liver without evidence of severe liver disease, such as ascites, encephalopathy, marked thrombocytopenia, bleeding esophageal varices; and with preserved hepatic synthetic function, (e.g., albumin ≥ 3.5 g/dL, total bilirubin ≤ 1.5 mg/dL, and prothrombin time international normalized ratio (INR) ≤ 1.5).

Decompensated cirrhosis is cirrhosis of the liver with evidence of significant liver disease, such as ascites, encephalopathy, marked thrombocytopenia, bleeding esophageal varices; and loss of liver synthetic function, e.g., albumin < 3.5 g/dL, total bilirubin > 1.5 mg/dL, and prothrombin time international normalized ration (INR) > 1.5.)

MELD or **Model for End-stage Liver Disease** is a validated disease severity index that uses age, creatinine, bilirubin, and prothrombin time to predict mortality.

PROCEDURES

1. HEPATITIS A - TRANSMISSION OF HAV INFECTION

HAV is transmitted fecal-orally and is acquired either by person-to-person contact or by the ingestion of contaminated food or water. Persons at risk for HAV infection include persons consuming contaminated food or water, men who have sex with other men, persons who inject illegal drugs, and persons with clotting disorders who require clotting-factor concentrates.

Newly infected persons are most contagious during the 2-week period before the onset of jaundice. The presence of diarrhea increases contagiousness. HAV can be stable in the environment for weeks to months.

The prevalence of prior HAV infection among incarcerated persons is estimated at 22% - 39%. The prevalence of risk factors for acquiring HAV infection, as well community origin, determine the prevalence of HAV infection for any given inmate population. American Indians, Alaskan Natives, and many persons from Latin America, Africa, the Middle East, China, and Southeast Asia, come from communities with endemic HAV infection where infection by early adulthood is the norm.

In the United States, newly acquired cases of HAV infection are declining, but clusters of hepatitis A cases continue to occur through community-wide outbreaks. The incidence of hepatitis A displays marked geographic variability with the highest rates occurring in the Western United States and in large urban areas among men who have sex with men. Institutional outbreaks of hepatitis A have primarily been limited to settings with children and have not involved correctional facilities.

2. HEPATITIS A - NATURAL HISTORY OF HAV INFECTION

The mean incubation period from infection with HAV until the onset of symptoms of acute hepatitis is 30 days (range: 15 - 50 days). Patients may present with jaundice, dark urine, nausea, diarrhea and severe malaise. Acute hepatitis A is usually a self-limited illness, but a small number of patients develop fulminant hepatitis. Chronic HAV infection and chronic hepatitis A do not occur.

3. HEPATITIS A - DIAGNOSIS

Acute hepatitis A is confirmed by a positive serum IgM anti-HAV titer that is detectable within 5 to 10 days after the onset of symptoms and persists up to 6 months after infection. All

inmates presenting with symptoms of acute hepatitis should be tested for the presence of IgM anti-HAV, unless evidence of previous HAV infection exists (IgG anti-HAV-positive or total anti-HAV-positive/IgM anti-HAV-negative).

4. HEPATITIS A - TREATMENT

Treatment efforts are supportive for acute hepatitis A, since effective antiviral therapy is unavailable. Fulminant acute hepatitis A may be complicated by protracted nausea and vomiting, dehydration, high fever, impaired consciousness, and liver failure.

5. HEPATITIS A - PREVENTION OF HAV INFECTION

Vaccine administration: Hepatitis A vaccine is an inactivated, highly immunogenic vaccine that is administered intramuscularly in the deltoid or gluteal (upper outer quadrant) muscle in a two-shot series, 6 - 12 months apart depending on the vaccine preparation. The two brands of hepatitis A vaccine (HAVRIX®: formulated with a preservative; and VAQTA®: formulated without a preservative) are equally effective and can be considered interchangeable. A bivalent combination vaccine, TWINRIX®, containing hepatitis A (HAVRIX®) and hepatitis B (ENGERIX-B®) antigens, is given on a 0, 1, 6 month schedule, and is equally effective. Vaccination of a person with previous immunity to HAV infection does not increase the risk of adverse events. Hepatitis A vaccine should not be administered to persons with hypersensitivity to alum or components of the vaccine.

Vaccine indications: The following inmates should be considered candidates for hepatitis A vaccination:

- Inmates with liver disease or cirrhosis;

- Inmates with chronic HBV and HCV infections (priority should be given to inmates with underlying liver disease);

- Inmates with clotting-factor disorders who are administered clotting-factor concentrates (especially solvent-detergent-treated preparations);

- Inmates returning to communities with a high incidence of HAV infection who are determined to be at risk of infection on a case-by-case basis;

- Certain at-risk inmates in the context of a hepatitis A outbreak.

NOTE: Prevaccination serologic screening for prior immunity to HAV infection by detecting IgG or total anti-HAV may be cost-effective for populations at high risk for previous HAV infection, such as certain Native American populations and foreign-born inmates from Latin America, Africa, Southeast Asia, and China where HAV infection is endemic, and among inmates 50 years of age or older.

NOTE: Hepatitis A vaccine is not routinely indicated or recommended for inmates workers who are plumbers or foodworkers.

NOTE: Postvaccination serologic testing for immunity is not indicated since the hepatitis A vaccine is highly protective.

6. HEPATITIS A - INFECTION CONTROL

Reporting: Each institution should have a surveillance system for notifiable infectious diseases in accordance with BOP policy. All cases of acute hepatitis A should be reported to State health authorities as required by all the States and the Commonwealth of Puerto Rico. Acute hepatitis A cases should also be reported to the Central Office HSD.

Containment: Inmates diagnosed with acute hepatitis A should be considered contagious three weeks before to 10 days after the onset of jaundice for containment and contact investigation purposes. Inmates diagnosed with acute hepatitis A should be managed in accordance with the following guidelines:

- Isolated in a single cell with separate sink and toilet (e.g. observation cell) until 10 days after the onset of jaundice and until clinically improving without diarrhea;

- Immediately removed from any assigned duties as a food handler;

- Counseled regarding the importance of strict hand washing and other practical infection control measures;

- Managed using standard precautions to prevent fecal-oral transmission when potentially in contact with contaminated body fluids, including wearing gloves or other personal protective equipment;

- Evaluated by a health care provider daily while acutely ill for signs and symptoms of liver failure such as change in mental status, vomiting, and dehydration.

Contact investigations: A contact investigation in consultation

with local or State public health authorities is required for all inmates with acute hepatitis A who were incarcerated during the incubation period in order to enhance case-finding of other inmates who may be potentially infected with HAV. All food handlers should be evaluated as part of the contact investigation. Public health officials should be directly involved in any potential foodborne outbreak to determine the need for broad-based immunoprophylaxis. A contact investigation tool is attached in **Appendix 1, Contact Investigation - Acute Hepatitis A.**

Post-exposure management:

- **Indications:** The following susceptible contacts of the index case should be considered for immunoprophylaxis:

  - cellmate(s);

  - sexual contacts;

  - persons routinely sharing toilet facilities;

  - very close contacts such as those who have shared eating utensils and cigarettes;

  - other food handlers if source-case was food handler;

  - broad-based immunoprophylaxis to inmate population if source-case was food handler (only on a case-by-case basis in consultation with local and State health care authorities).

- **Administration:** Post-exposure prophylaxis is provided by passive immunization with pooled serum immunoglobulin (IG) in accordance with the following guidelines:

  - Screening for IgG (or total) anti-HAV is not recommended so that prophylaxis is not delayed;

  - IG is administered 0.02 mL/kg intramuscularly in the gluteal or deltoid muscle (single dose);

  - IG prophylaxis is not effective unless administered within 2 weeks of exposure;

  - Persons with prior hepatitis A vaccination or previously documented natural immunity (IgG anti-HAV+) do not require prophylaxis;

  - Hepatitis A vaccination is not recommended for post-exposure

prophylaxis. Hepatitis A vaccination may be indicated for inmate populations determined to be a potential future risk of exposure in the context of an investigated outbreak.

7. HEPATITIS B - TRANSMISSION OF HBV INFECTION

HBV is a bloodborne pathogen that is spread through percutaneous and mucosal exposures to infected blood and body fluids that contain blood. Major modes of acquiring HBV infection include injection drug use, sexual intercourse with an infected partner, perinatal transmission from mother to child, chronic hemodialysis, and, certain occupational exposures. Tattooing with shared, contaminated needles or needle-like devices in jails and prisons is another potential mode of HBV transmission, that specifically affects inmate populations. HBV is viable for at least seven days on environmental surfaces.

HBV is commonly transmitted either perinatally or during childhood in parts of the world where the infection is endemic, such as in Asia, the South Pacific, sub-Saharan Africa, and certain populations in the Arctic, South America, and the Middle East.

Persons with chronic hepatitis B infection (HBsAg-positive) although often asymptomatic, can transmit HBV to others. Contagiousness is increased in persons with chronic HBV infection who are also hepatitis B e antigen-positive (HBeAg-positive).

Outbreaks of acute hepatitis B have occurred in the correctional setting. Infected contacts may be asymptomatic and identified only through contact investigations.

8. HEPATITIS B - ACUTE HBV INFECTION (DIAGNOSIS/NATURAL HISTORY)

The incubation period of HBV infection from transmission until the onset of symptoms averages between 90 to 120 days (range: 45 - 180 days). Acute hepatitis B occurs in approximately 30% to 50% of infected adults and may be mild, severe, or fulminant. Signs and symptoms of acute hepatitis include fever, jaundice, nausea, abdominal pain, and malaise. Arthritis, serum sickness, and a nonspecific rash may also occur with acute HBV infection and, when present, are helpful diagnostically.

Acute HBV infection is confirmed by the serologic detection of IgM anti-HBc and HBsAg. The detection of HBsAg alone is not diagnostic for acute HBV infection, since persons with asymptomatic chronic HBV infection can be newly infected with other pathogens that cause acute hepatitis. **NOTE**: IgM anti-HBc may persist at detectable levels for up to 2 years in a small

subset of acutely infected persons.

9. HEPATITIS B - CHRONIC HBV INFECTION (SCREENING)

Newly incarcerated inmates should be provided educational information on the transmission, natural history, and medical management of HBV infection by appropriately trained personnel in accordance with BOP policy. The BOP peer-oriented video on infectious diseases, the attached information in **Appendix 2, Inmate Fact Sheet on Hepatitis B and C Viral Infections** and other appropriate patient educational tools can be used to facilitate counseling efforts.

Screening method: Screening for HBV infection should be performed by measuring HBsAg (additional HBV serologic tests may be warranted depending on the inmate's medical history)

Non-sentenced inmates: Screening for HBV infection in asymptomatic, highly mobile, non-sentenced inmates in BOP detention facilities should only be pursued for specific medical indications such as inmates who are pregnant or have signs or symptoms of acute or chronic hepatitis. Asymptomatic non-sentenced inmates in BOP detention facilities with histories of injection drug use or other high risk behaviors for HBV infection should be counseled regarding their risk of acquiring HBV infection and the behaviors that will reduce transmission of HBV infection to themselves and others during incarceration and upon release. Referrals to community testing sites should be made when appropriate.

Long-term inmates in BOP detention facilities should be screened for HBV infection in accordance with guidelines for sentenced inmates.

Sentenced inmates: The following sentenced inmates should be screened for HBV infection:

- Pregnant inmates (**NOTE**: Routine screening is medically imperative regardless of previous screening results due to the risk of perinatal transmission);

- Inmates with histories of percutaneous exposures to potentially infected blood, such as injection drug use or receiving tattoos or body piercings while in jail or prison;

- Inmates with HIV or HCV infections;

- Asymptomatic inmates with elevated ALT levels of unknown

etiology;

- Inmates with high risk behaviors for HBV infection;

- Inmates from countries with extremely high rates of infection (e.g., Africa, Eastern Europe, the Western Pacific and all of Asia with the exception of Japan);

- Inmates on chronic hemodialysis who fail to develop antibodies after two series of vaccinations should be screened monthly (i.e., measure HBsAg);

- As clinically indicated, (e.g. inmates with signs or symptoms of acute or chronic hepatitis).

NOTE: Sentenced inmates who have risk factors for chronic HBV infection, but who initially refuse testing, should be counseled periodically regarding the need for testing during routine patient encounters.

10. HEPATITIS B - CHRONIC HBV INFECTION (DIAGNOSIS/COUNSELING)

Diagnosis: The diagnosis of chronic HBV infection is confirmed by the serologic detection of hepatitis B surface antigen (HBsAg) on two separate occasions ≥ 6 months apart; or the one time detection of HBsAg, along with total anti-HBc-positive/IgM anti-HBc-negative.

A complicated array of HBV serologic markers are useful, alone or in combination, in characterizing various phases of HBV infection. Serologic markers are outlined in **Appendix 3, Interpretation of Hepatitis B Virus Serologic Markers.**

Patient counseling: Inmates diagnosed with chronic HBV infection should be counseled by a health care provider about the natural history of the infection, potential treatment options, and specific measures for preventing transmission of HBV infection to others (during incarceration and upon release), including the following information and recommendations:

- Most persons with HBV infection will remain healthy, but a small number of persons will develop serious liver disease. Talk to your health care provider about your personal health status;

- Drug treatment options for chronic hepatitis B are developing. Medications may or may not be appropriate for you at this time. Talk to your doctor about your specific treatment plan;

- Do not shoot drugs, have sex with other inmates, or get a

tattoo or body piercing while in prison;

- Do not share personal items that might have your blood on them, such as toothbrushes, dental appliances, nail-grooming equipment or razors;

- Cover your cuts and skin sores to keep your blood from contacting other persons;

- Before release, talk to a health care provider about specific ways you can reduce the risk of transmitting HBV infection to others after you are released;

- Upon release, markedly limit alcohol consumption or abstain altogether, and speak to a physician prior to taking any new medications, including over-the-counter drugs such as nonsteroidal anti-inflammatory agents and herbal remedies, that may damage your liver;

- Upon release, do not donate blood, body organs, other tissue or semen;

- Upon release, seek medical attention so that your condition is appropriately monitored and treated.

11. HEPATITIS B - CHRONIC HBV INFECTION (NATURAL HISTORY)

The majority of adults acutely infected with HBV eventually clear HBsAg from the blood and develop antibodies to HBsAg (anti-HBs) that confer long-term protection from reinfection. A subset of persons acutely infected with HBV develop chronic HBV infection (HBsAg-positive for 6 months or longer). The risk of chronic HBV infection is much greater for persons from parts of the world where HBV is endemic and acquired perinatally, such as in Asia with the exception of Japan. Immunosuppressed individuals are also more likely to develop chronic HBV infection.

Chronic HBV infection evolution: Persons with chronic HBV infection (HBsAg-positive) may develop **(1) chronic hepatitis, or (2) asymptomatic chronic infection, or (3) resolve their infection spontaneously:**

- **Chronic hepatitis B** is diagnosed by the following four criteria: **(1)** HBsAg-positive for > 6 months; **(2)** Serum HBV DNA > 10^5 cps/mL; **(3)** persistent or intermittent elevations in ALT levels; and **(4)** liver biopsy showing necroinflammation score of Knodell ≥ 4).

NOTE: HBV DNA assays are poorly standardized and should be interpreted cautiously. The diagnostic criteria for serum HBV DNA of 10^5 cps/mL is somewhat arbitrary, but helps to identify patients with significant infection that is usually associated with liver inflammation.

Chronic hepatitis B can be **HBeAg-positive or HBeAg-negative.** Persons with HBeAg-positive hepatitis are at risk of progressive liver disease; however, over time, the majority of these patients spontaneously develop antibodies to HBeAg (anti-HBe), and have a chronic asymptomatic infection. Persons with HBeAg-negative chronic hepatitis B, have elevated HBV DNA levels and necroinflammation on liver biopsy despite being HBeAg-negative. HBeAg-negative chronic hepatitis has a fluctuating, less predictable course and occurs more commonly in persons from Asia and Mediterranean countries.

- **Chronic asymptomatic HBV infection:** Certain persons with chronic HBV infection are able to clear HBeAg, associated with a decrease in detectable serum HBV DNA, while remaining HBsAg-positive. They have the following diagnostic criteria: **(1)** HBsAg-positive for > 6 months; **(2)** HBeAg-negative/anti-HBe-positive; **(3)** serum HBV DNA < 10^5 cps/mL; **(4)** persistently normal ALT levels; and **(5)** liver biopsy confirms absence of significant necroinflammation with a Knodell score <4. These persons with chronic HBV infection are at low risk of developing decompensated cirrhosis.

- **Resolved hepatitis B:** A certain proportion of persons with chronic HBV infection spontaneously clear their infection (approximately 0.5% yearly). Serum HBV DNA levels decrease to undetectable levels (although very low levels may be detectable by PCR), ALT levels normalize, and serum HBsAg disappears.

Chronic hepatitis B flares: Clinically apparent flares of hepatitis can occur in persons with chronic HBV infection during the following: spontaneous clearance of HBeAg with development of anti-HBe antibodies, following HBV-HDV (hepatitis delta virus) superinfection, with immunosuppression, and following antiviral therapy for chronic hepatitis B.

Chronic hepatitis B complications: Individuals with chronic HBV infection are at increased risk of developing decompensated cirrhosis and hepatocellular carcinoma (HCC). Rates of progression to cirrhosis or HCC are affected by a variety of factors, including: HBeAg positivity, history of alcoholism, co-infections with HIV, HCV, or HDV, and family history of HCC. Nonhepatic complications of HBV infection include membranous

glomerulonephritis and polyarteritis nodosa.

12. HEPATITIS B - EVALUATION AND TREATMENT OF HBV INFECTIONS

Acute hepatitis B: Treatment efforts are primarily supportive for acute hepatitis B. Fulminant disease, suggested by hemodynamic instability, dehydration, delirium, vomiting, and a rapidly receding liver edge, requires hospitalization and intensive management. Inmates with acute hepatitis B should be monitored during convalescence and thereafter to determine if they develop chronic HBV infection (persistently HBsAg-positive) or clear their infection (anti-HBs-positive).

Baseline evaluation (chronic HBV infection): A baseline clinician evaluation should is indicated for inmates who have chronic HBV infection (HBsAg-positive) and should include:

- Targeted history (assess age of initial infection, alcohol and substance abuse history, family history of hepatocellular carcinoma and chronic HBV infection, risks for gastrointestinal bleeding, and symptoms of decompensated cirrhosis);

- Targeted physical examination (assess for evidence of decompensated cirrhosis, such as jaundice, ascites, encephalopathy, asterixes, and peripheral edema);

- Serum ALT, AST, bilirubin, alkaline phosphatase, albumin, prothrombin time, and further diagnostic evaluations as clinically warranted for other potential causes of liver disease, such as hemochromotosis, Wilson's disease, and autoimmune hepatitis;

- CBC with differential and platelet count;

- Renal function assessment (i.e., serum creatinine/BUN);

- HBeAg, anti-HBe;

- HBV DNA nucleic acid test (**NOTE:** HBV DNA assays are poorly standardized; therefore data should be interpreted cautiously);

- Screening for anti-HIV, anti-HCV, and anti-HDV;

- Hepatitis A vaccination (Priority should be given to inmates with underlying liver disease. Prescreening for immunity to HAV, by detecting IgG (or total) anti-HAV, should be considered prior to vaccination for Native American populations and foreign-born inmates from Latin America, Africa, Southeast Asia, and China where HAV infection is endemic, and for inmates 50 years of age

or older.)

Hepatocellular carcinoma (HCC) screening: HCC occurs in persons with chronic HBV infection with or without cirrhosis. The optimal HCC screening strategy for patients with chronic HBV infection is uncertain. The following screening strategy should be considered based on available data, in conjunction with case-by-case decision-making:

- Screen the following inmates with chronic HBV infection who are at higher risk for HCC by periodically obtaining a liver ultrasound (e.g., annually) and alpha-fetoprotein (e.g., every 6 months);

- Inmates with cirrhosis;

- Inmates with a family history of HCC;

- Male inmates > 45 years of age;

- Obtain a baseline alpha-fetoprotein screen for otherwise low-risk inmates from countries where chronic HBV infection is endemic and consider periodic repeat alpha-fetoprotein screening (e.g., annually).

Periodic evaluations (chronic HBV infection): Clinician evaluations for inmates with chronic HBV infection should be scheduled on a case-by-case basis in consideration of the following:

- **Chronic HBV infection with elevated ALT levels (HBeAg-positive or HBeAg-negative/HBV DNA-positive)**: Refer for liver biopsy and possible antiviral therapy and monitor as clinically necessary.

- **HBeAg-positive with normal ALT levels**: Monitor ALT levels every 3 - 6 months/HBeAg annually to determine if patient is developing worsening liver disease or clearing HBeAg (**NOTE**: ALT levels may transiently increase with clearance of HBeAg and the development of anti-HBe).

- **HBeAg-negative/HBsAg-positive (asymptomatic chronic HBV infection)**: Monitor ALT levels every 6 - 12 months/HBsAg annually for spontaneous clearance, i.e., resolution of infection (HBsAg-negative).

- **Resolved chronic HBV infection**: Chronic care clinic evaluations and ongoing monitoring of ALT levels and hepatitis B serologies are not required since the infection has been cleared.

Considerations and evaluation strategy for treatment: A thoughtful approach to initiating antiviral therapy for chronic hepatitis B is warranted, since **(1)** current treatment options have uncertain long-term efficacy; **(2)** up to 25% of patients spontaneously clear HBV infection without therapy in placebo-controlled trials; and **(3)** future treatment options may more effective and better defined.

The decision to recommend antiviral treatment should be based on the severity of liver disease, the likelihood of response, existing co-morbid conditions, the potential for adverse reactions, and other relevant patient-specific factors. A strategy for evaluating inmates with chronic HBV infection for antiviral therapy is outlined in **Appendix 4, Evaluation Strategy for the Treatment of Chronic Hepatitis B.**

Treatment indications for chronic hepatitis B: Indications for antiviral therapy include the following criteria:

- Chronic HBV infection (HBsAg-positive) documented for at least 6 - 12 months duration;

- Evidence of active viral replication (HBeAg-positive/HBV DNA-positive OR HBeAg-negative/HBV DNA-positive);

- Chronic liver inflammation suggested by elevated ALT levels above upper limit of normal;

- Evidence of necroinflammation on liver biopsy with a score ≥ 4.

Prior to initiating antiviral therapy for chronic hepatitis B, inmates should be evaluated by a physician and screened for complicating co-morbid conditions or other causes of liver disease, including the following: anti-HIV, anti-HCV, anti-HDV, anti-nuclear antibodies (ANA), serum ferritin, pregnancy test for female inmates, and other diagnostic tests as indicated.

A psychiatrist or psychologist evaluation and thyroid function studies are indicated prior to interferon therapy.

Antiviral treatment options for chronic hepatitis B: Interferon alfa, lamivudine, and adefovir are approved by the Food and Drug Administration (FDA) for the treatment of chronic hepatitis B. Drug dosages and side effects are outlined in **Appendix 5, Antiviral Medications for Chronic Hepatitis B.** Specific drug treatment recommendations should be patient-specific with specialist consultation as necessary.

Drug class considerations include the following:

- **Interferon treatment (Roferon-A, Intron-A):** Interferon alfa treatment for chronic hepatitis B is prescribed as 5 million units daily or 10 million units thrice weekly given by subcutaneous injection for 16 - 24 weeks for HBeAg-positive patients. HBeAg-negative patients require 12 months therapy or longer (The optimal duration of therapy in these patients is uncertain). Prednisone priming before initiating therapy is **NOT** recommended. The average response rate to interferon treatment of chronic hepatitis B (HBeAg-positive) is 30 - 40%. Predictors of a favorable response to interferon therapy include the following factors:

- Short duration of disease;

- High pretreatment ALT levels;

- Low serum HBV DNA levels;

- Liver necroinflammation on biopsy;

- Absence of renal failure, HIV infection, or other serious co-morbidity.

NOTE: HBeAg-positive responders to interferon treatment usually clear hepatitis B e antigen, but viremia may persist and the long-term clinical outcomes are uncertain.

NOTE: Persons with HBeAg-negative/HBV DNA-positive chronic hepatitis B are have lower response rates than HBeAg-positive patients.

NOTE: Interferon is contraindicated in patients with decompensated cirrhosis since life-threatening complications can occur. Interferon should be used very cautiously in patients with compensated cirrhosis since clinical deterioration may occur.

- **Interferon side-effects:** An influenza-like reaction often occurs within 6 - 8 hours of initial treatment with interferon. Fatigue, headache, fever, and myalgias occur commonly. This acute reaction may abate with subsequent treatments and can be partially aborted by premedication with antipyretics. Acetaminophen can be given safely up to 2 gm/day in divided doses. Nonsteroidal anti-inflammatory agents (NSAIDS) should not be prescribed.

Chronic side effects of interferon can include severe fatigue, weight loss, reversible alopecia, irritability, rage, confusion, and neuropsychiatric disorders. Severe and incapacitating depression can occur, even in persons without previous histories of depression. Bone marrow suppression resulting in neutropenia and thrombocytopenia are potentially serious effects of interferon that should be anticipated and monitored closely particularly in patients with cirrhosis or HIV infection. Thyroid dysfunction occurs in approximately 4% of persons treated with interferon and may result in irreversible thyroid dysfunction, even with cessation of drug therapy.

Inmates with side effects to interferon should have their dosage reduced or therapy discontinued depending on the severity of the side effects. Serious sequelae may occur in fewer than 1% of persons receiving interferon treatment and can include: renal failure, pneumonitis, severe bone marrow suppression, visual and hearing loss, retinal hemorrhage, acute psychosis, and suicide.

- **Lamivudine (Epivir HBV®):** Lamivudine is prescribed orally, 100 mg/day for at least 1 year for the treatment of chronic hepatitis B. In persons who are HBeAg-positive, the endpoint of treatment is seroconversion, i.e., the development of anti-HBe. Treatment beyond one year without seroconversion is of uncertain benefit in these patients.

Lamivudine treatment is generally very well tolerated with milder adverse effects than interferon, although serious adverse events including lactic acidosis, hepatomegaly with steatosis, and pancreatitis occur rarely. Lamivudine is renally excreted and dosing, must be adjusted based on creatinine clearance.

NOTE: Lamivudine may have some efficacy in treating patients with end-stage liver disease for whom interferon is either contraindicated or potentially harmful, i.e., decompensated or compensated cirrhosis respectively.

NOTE: Lamivudine is prescribed at a higher dose (150 mg PO BID) for individuals co-infected with HIV, in the context of a multi-drug antiretroviral regimen.

NOTE: The potential benefits of lamivudine therapy are limited by the frequent development of drug resistance. Resistance to lamivudine can develop despite adherence to therapy. The clinical course of patients with chronic hepatitis B and lamivudine resistance is variable and unpredictable. Some patients who develop lamivudine resistance present with acute exacerbations of liver disease, while others develop only elevated HBV DNA and ALT levels comparable to pretreatment

values.

- **Adefovir (Hepsera®):** Adefovir dipivoxil, a nucleotide analogue, is prescribed as a 10 mg oral daily dose for the treatment of chronic hepatitis B. Treatment with adefovir results in histologic improvement in liver disease in approximately 50% of patients without the development of drug resistance. Both HBeAg-positive/HBV DNA-positive and HBeAg-negative/HBV DNA-positive patients may benefit from adefovir therapy. The optimal duration of treatment is uncertain (but is at least 48 weeks) and should be determined on a case-by-case basis.

NOTE: Severe exacerbations of hepatitis may occur when adefovir is discontinued; therefore, these patients should be monitored closely. Patients should be screened for renal insufficiency and HIV infection prior to initiating therapy.

NOTE: Adefovir is generally well tolerated at the 10 mg dose and is not readily associated with the renal toxicity observed at higher doses; however, persons with underlying renal insufficiency remain at increased risk for nephrotoxicity. Potential complications of adefovir therapy include idiosyncratic lactic acidosis and hepatomegaly, and resistance to HIV in persons with undiagnosed or untreated HIV infection.

Treatment of chronic hepatitis B with co-morbid conditions: Inmates with chronic hepatitis B and the following co-morbid conditions warrant special consideration:

- **HBV and HCV co-infection:** Antiviral therapy in this setting should only be initiated after consultation with a specialist, and with great caution, due to the lack of a recommended treatment strategy and the uncertain effects on underlying liver disease;

- **HBV and HIV co-infection:** Antiviral treatment for persons with HBV and HIV infections should be initiated cautiously in consultation with physician experts as necessary. Lamivudine or adefovir treatment in patients co-infected with HIV should only be initiated along with a multi-drug highly active antiretroviral regimen;

- **Renal disease:** Renal insufficiency secondary to glomerulonephritis from HBV infection may respond to interferon therapy, however treatment should be considered in consultation with a physician expert and dosage adjustments made as necessary. Neither adefovir nor lamivudine should be used to treat chronic hepatitis B in patients with renal insufficiency.

Monitoring inmates treated with antiviral therapy for chronic hepatitis B:

Inmates should receive clinician evaluations during antiviral therapy for chronic hepatitis B that are generally consistent with the following:

- Clinician evaluations weekly for one month, then monthly thereafter, to assess drug side effects and potential disease complications;

- Psychiatry or psychology evaluations as clinically indicated during interferon treatments;

- ALT at weeks 1, 2, and 4, and at 4 - 8 week intervals thereafter;

- Periodic bilirubin, prothrombin time and other liver function studies as clinically warranted;

- Creatinine and BUN periodically, monthly while on adefovir;

- CBC with differential and platelet count at weeks 1, 2, and 4 and at 4 - 8 week intervals thereafter;

- Thyroid function studies every 3 months during interferon therapy.

NOTE: Transient increases in aminotransferase levels are common during therapy and correlate with immune system clearance of HBV and the disappearance of HBeAg. Mild to moderate increases in liver enzymes should not be an indication for reducing or discontinuing interferon therapy, unless associated with deteriorating liver synthetic function or jaundice.

Discontinuation of antiviral therapy for chronic hepatitis B:
Antiviral therapy for chronic hepatitis B should be discontinued in consultation with a specialist. Severe exacerbations of liver disease can occur with the cessation of antiviral therapy, including adefovir. The effectiveness of treatment is determined by measuring the following parameters 6 months after the completion of antiviral therapy:

- Absence of HBeAg;

- Absence of HBV DNA;

- Normalization of ALT.

NOTE: HBeAg may not disappear for months or longer after the completion of effective antiviral therapy. HBsAg may remain positive and HBV DNA may remain detectable for years after completion of treatment. The long-term clinical consequences of persistent viremia are uncertain.

13. HEPATITIS B - PREVENTION

Vaccine programming and indications: Each institution should establish a hepatitis B vaccine program for inmates. The BOP is currently targeting the following inmates for hepatitis B vaccination based on risk of infection and co-morbid conditions:

- Inmates on chronic hemodialysis or inmates with evolving end-stage renal disease for whom future hemodialysis is anticipated;

- Pregnant women (previously unvaccinated HBsAg-negative mothers);

- As a component of post-exposure prophylaxis for unprotected inmates following percutaneous or permucosal exposures to blood;

- Inmate workers at risk for bloodborne pathogen exposure in accordance with the institution's exposure control plan and applicable federal regulations;

- Contacts of inmates diagnosed with acute hepatitis B in the context of a contact investigation;

- Inmates with HIV infection with risk factors for acquiring HBV infection;

- Inmates with chronic HCV infection (priority should be given to inmates with liver disease);

- Inmates with cirrhosis or liver disease;

- Inmates at risk for HBV infection due to a history of high risk behaviors, such as injection drug use, unprotected sex with multiple partners, and men who have sex with men.

Vaccine administration: Hepatitis B vaccine is available as ENGERIX-B® or RECOMBIVAX HB®. The products are interchangeable; i.e., a vaccination series begun with one product may be completed with the other. Hepatitis B vaccine is also available in a combined formulation with hepatitis A vaccine, TWINRIX®. Viral hepatitis vaccines are listed in **Appendix 6, Viral Hepatitis Vaccine Doses and Schedules**. Hepatitis B vaccination should be administered in accordance with the following

guidelines:

- Prevaccination serologic screening for immunity to HBV infection is not routinely recommended, but should be considered on a case-by-case basis. Serologic screening is only cost-effective if the probability of prior immunity is high, such as in inmates who have undocumented prior hepatitis B vaccination (screen for anti-HBs) and in inmates from countries where HBV infection is endemic (e.g., such as in Asia, the South Pacific, sub-Saharan Africa, and certain populations in the Arctic, South America, and the Middle East);

- A previous anaphylactic reaction to baker's yeast or previous vaccination, is a contraindication to vaccination or booster vaccination;

- Pregnancy should not be considered a contraindication to vaccination for women at risk of acquiring HBV infection, since HBV itself poses a significant risk to the fetus or newborn. (**NOTE:** No apparent risk exists for adverse effects to developing fetuses when hepatitis B vaccine is administered to pregnant women. Pregnant inmates who are candidates for vaccination should be counseled regarding the risks and benefits of vaccination during pregnancy.)

- All inmate candidates for vaccination should receive counseling by a physician or otherwise qualified health care provider on the administration and potential adverse reactions of hepatitis B vaccination. Counseling, consent, and declination should be documented as per BOP policy;

- The three-dose vaccination series is ideally administered at 0, 1, and 4 - 6 months, however there is significant flexibility with the administration of the complete series with the following guidelines: there must be at least a 1 month interval between doses #1 and #2; and at least a 2 month interval between doses #2 and #3; and at least a 4 month interval between doses #1 and #3. If a dose is delayed the next dose should be administered without restarting the entire series;

- The vaccine is administered intramuscularly in the **deltoid** muscle;

- Postvaccination testing (anti-HBs) to determine antibody responder status is not routinely indicated for newly vaccinated inmates unless future exposures to HBV are anticipated, e.g, inmates receiving hemodialysis and certain inmate workers.

Inmate workers: Inmates workers with potential exposures to

infectious blood or body fluids as determined by the institution's bloodborne pathogen exposure control plan should be offered hepatitis B vaccination in accordance with BOP policy. Newly vaccinated inmate workers should have anti-HBs levels measured 1 - 2 months after the third dose of vaccine. Inmates with low levels of anti-HBs (< 10 mIU/mL) should receive a second three-dose hepatitis B vaccine series with repeat antibody testing 1 - 2 months after the third dose of vaccine. Inmate workers who still have low levels of anti-HBs after receiving the second hepatitis B vaccine series should be considered nonresponders susceptible to HBV infection and should be counseled regarding appropriate preventive measures and the need for post-exposure HBIG prophylaxis despite vaccination.

Hemodialysis patients: Inmates on chronic hemodialysis are at risk for ongoing exposures to HBV and require hepatitis B vaccination along with close monitoring of their immune status in accordance with the following:

- Inmates on hemodialysis require higher doses of hepatitis B vaccine that are subject to different administration schedules compared to standard hepatitis B vaccine recommendations as enumerated in **Appendix 6**.

- Inmates on hemodialysis who are newly vaccinated for hepatitis B should have anti-HBs measured 1 - 2 months after the last dose of vaccine. Inmates with low levels of anti-HBs (< 10 mIU/mL) should receive a second hepatitis B vaccine series with repeat antibody testing 2 months after the last dose of vaccine. If anti-HBs levels remain low, the inmate should be considered a nonresponder, susceptible to HBV infection and should be counseled regarding appropriate preventive measures. Nonresponders and susceptible inmates who refuse vaccination should be monitored for newly acquired HBV infection while on dialysis by measuring HBsAg, monthly.

- Inmates on hemodialysis with adequate anti-HBs (≥ 10 mIU/mL) following vaccination, but who are anti-HBc negative, should have anti-HBs monitored on an annual basis. A booster dose of vaccine should be administered if the anti-HBs falls below 10 mIU/mL.

- Inmates on hemodialysis with a history of HBV infection (anti-HBc-positive and anti-HBs-positive or HBsAg-positive) do not require anti-HBs monitoring or consideration for vaccination.

- Inmates receiving hemodialysis who test positive for anti-HBc alone could have a false positive test, low-grade chronic infection, remote infection, or resolving acute infection. These hemodialysis patients should be evaluated in accordance with CDC

guidelines, per the algorithm in *MMWR* 2001;50(RR-5), to assess their status so that the appropriate monitoring, immunization, and infection control measures can be determined.

14. HEPATITIS B - INFECTION CONTROL

Patient education: All inmates should be counseled during orientation to the institution and when appropriate during clinical evaluations of the importance of preventing blood exposures to others during activities of daily living such as sharing toothbrushes and razors and through unsafe behaviors such as injection drug use, tattooing, and sexual contact with other inmates.

Reporting: Each institution should have a surveillance system for notifiable infectious diseases in accordance with BOP policy. All cases of acute hepatitis B, should be reported to State health authorities as required by all States and the Commonwealth of Puerto Rico. Inmates with chronic HBV infection should be reported to the local and State authorities, as required. All acute cases of hepatitis B and any HBsAg seroconversions among hemodialysis patients should be reported to the Central Office HSD.

Containment: Inmates with acute hepatitis B and chronic HBV infection (HBsAg-positive) do not require isolation, but should be counseled on the specific measures necessary for preventing further transmission of HBV to others during incarceration and upon release and should be managed while incarcerated using standard infection control precautions. Non-disposable patient-care items must be appropriately cleaned, disinfected, or sterilized based on the use; and measures must taken to prevent cross contamination during patient care, e.g., dialysis, vascular access, cauterizing, dental procedures, etc., in accordance with CDC guidelines.

Hemodialysis: Infection control measures should be implemented to reduce the transmission of HBV during hemodialysis in accordance with CDC guidelines, i.e., Recommendations for preventing transmission of infection among chronic hemodialysis patients, *MMWR*, 2001;50(RR-5), that include the following:

- **Screening and prevention**: All inmates receiving chronic hemodialysis should be screened for prior HBV infection before admission to the hemodialysis unit by measuring the following serologic markers: HBsAg, total anti-HBc, and anti-HBs. Inmates susceptible to HBV infection should receive hepatitis B vaccine in accordance with CDC guidelines. All inmates who remain susceptible to HBV infection, i.e, nonresponders, should be

screened monthly for HBsAg seroconversion, both as a patient care and surveillance measure.

- **Infection control measures:** Institutions that provide dialysis should establish written policies and practices and a mechanism for review, update, and training of staff to ensure that infection control measures to reduce the transmission of HBV during hemodialysis are implemented including the following:

  - The use of specifically assigned stations or isolation room, chairs, medications, supplies, and designated staff (do not care for HBV-susceptible inmates at the same time) to separate HBsAg-positive inmates from HBsAg-negative inmates;

  - HBsAg-positive inmates should be dialyzed on specifically dedicated machines. Dialyzers from HBsAg-positive inmates should not be reused;

  - If it is necessary to reuse a machine used by a HBsAg-positive inmate for a HBsAg-negative inmate, internal pathways of the machine can be disinfected using conventional protocols and extreme surfaces cleaned using soap and water or a detergent germicide;

  - All machines and station areas that are used on HBsAg-positive inmates must be terminally cleaned after each use (refer to manufacturers' instructions and CDC recommendations.

Contact investigations: A contact investigation is required for for inmates diagnosed with acute hepatitis B (IgM anti-HBc-positive), who were incarcerated during the 6 weeks - 6 months prior to disease onset, in order to identify other inmates acutely infected with HBV and better target post-exposure management of asymptomatic contacts. Close contacts should be tested for HBsAg to help identify the source-case. Aggressive "ring vaccination" of close contacts is warranted. The contact investigation should be coordinated with local and State health departments. A contact investigation tool is attached in **Appendix 7, Contact Investigation - Acute Hepatitis B.**

Asymptomatic inmates with positive IgM anti-HBc serologies should be first evaluated to assess if the inmate was symptomatic with acute hepatitis B or infected with HBV before or after incarceration. (IgM anti-HBc can remain positive up to two years after acute infection.) A contact investigation should be pursued if HBV infection was acquired while the inmate was incarcerated. If the infection was acquired prior to incarceration the local and State health authorities should be notified as required.

NOTE: Inmates diagnosed with chronic HBV infection (HBsAg-positive) should be interviewed at the time of diagnosis and periodically thereafter during chronic care visits to determine if they have exposed other inmates to infected blood through sharing toothbrushes and razors, through injection drug use, tattooing, or sexual contact with other inmates. Identified contacts should be considered for post-exposure prophylaxis.

Post-exposure management: Inmates with percutaneous (e.g., injection drug use, tattooing, injury with needle or needle-like device contaminated with blood of unknown origin) or mucosal (e.g., sexual contact, human bites) exposures to blood warrant emergent evaluation for post-exposure prophylaxis. **NOTE**: In evaluating human bites, both the person bitten and the biter should be considered exposed to blood.

- **Emergent care**: Wounds and skin sites that have been in contact with blood or bloody body fluids should be washed with soap and water. Exposed mucous membranes should be flushed with water. Squeezing the wound and treating with topical antiseptics are not recommended.

- **Counseling**: Inmates with percutaneous or mucosal exposures to blood should be assessed by a health care provider and counseled regarding their risk of HBV infection, the natural history of HBV infection, and the recommendations for post-exposure prophylaxis.

- **Post-exposure interventions**: Prompt post-exposure prophylaxis should be provided to inmates potentially exposed to HBV in accordance with the following:

  - Unvaccinated inmates should begin the vaccine series immediately and subsequent doses should be administered in accordance with standard practices. Exposed inmates who have already begun, but not completed the vaccine series, should receive subsequent vaccine doses as previously scheduled;

  - The source of the exposure should be tested for HBsAg, even if that person was previously vaccinated;

  - If the source of the exposure is HBsAg-positive, hepatitis B immunoglobulin (HBIG) 0.06 mL/kg body weight should also be administered to unvaccinated exposed inmates, as soon as possible but ≤ 7 days after the exposure. (**NOTE**: When administered simultaneously, hepatitis B vaccine and HBIG should be given intramuscularly at separate sites, with the vaccine administered in the deltoid muscle);

  - Inmates who have been fully vaccinated prior to an exposure

to HBV ordinarily do not require post-exposure prophylaxis;

- Inmates who have been fully vaccinated prior to an exposure to HBV may warrant a vaccine booster and/or HBIG, as outlined in **Appendix 8, Management of HBV Exposures,** if their anti-HBs responder status has previously been determined (e.g., hemodialysis patients, certain inmate workers); or their responder status is newly assessed because of unique circumstances surrounding the exposure;

- In the context of a contact investigation of acute hepatitis B cases, both hepatitis B vaccination and HBIG are indicated for inmates who have had percutaneous or mucosal exposures to blood; whereas hepatitis B vaccination alone is indicated for other close inmate contacts who have not had direct percutaneous or mucosal exposures.

15. HEPATITIS C - TRANSMISSION OF HCV INFECTION

HCV is a single-stranded, enveloped, RNA virus with 6 genotypes and more than 50 subtypes. Genotype 1 is predominant in the United States.

HCV is transmitted primarily by direct percutaneous exposures to infectious blood such as through injection drug use or the transfusion of contaminated blood products (prior to screening in July 1992). HCV is inefficiently transmitted through sexual contact; however, persons with a history of sexually transmitted diseases and/or multiple sexual partners have an increased risk of acquiring HCV infection. HCV is transmitted from mother to child in approximately 4% - 7% of pregnant women who have chronic HCV infection at the time of delivery. Breast-feeding does not transmit HCV from an infected mother to her child. Tattooing with shared, contaminated needles or needle-like devices in jails and prisons is a potential mode of HCV transmission that may affect inmate populations. Intranasal cocaine use may be a risk factor for acquiring HCV infection, but its exact role in transmission remains ill-defined. HCV is not spread by sneezing, hugging, coughing, food or water, sharing eating utensils or drinking glasses, or through other casual contact.

16. HEPATITIS C - ACUTE HCV INFECTION (DIAGNOSIS)

The mean incubation time from the transmission of HCV infection to the onset of symptoms is 6 - 7 weeks (range: 2 - 26 weeks), however, only 20% - 30% of newly infected persons are symptomatic. Acute hepatitis C is rarely severe, but patients may be ill with jaundice, nausea, anorexia, and malaise. Serum ALT levels increase 4 to 12 weeks after acute HCV infection.

Antibodies to HCV may or may not be present when symptoms develop or with elevations in ALT levels, however, after 3 months of HCV infection, anti-HCV in detectable by immunoassay in 90% of patients.

The diagnosis of acute hepatitis C is confirmed by: **(1)** marked elevations in ALT with or without symptoms of acute hepatitis; **(2)** negative tests for acute hepatitis A (IgM anti-HAV) and acute hepatitis B (IgM anti-HBc); and **(3)** a positive anti-HCV screening immunoassay that is confirmed by supplemental testing (RIBA) or a high immunoassay signal-to-cut-off ratio. HCV RNA may be detected by a nucleic acid test (NAT) in the blood 1 to 3 weeks after exposure, but viremia may be transient, i.e., a negative NAT for HCV RNA does not preclude acute HCV infection.

17. HEPATITIS C - CHRONIC HCV INFECTION (SCREENING)

Newly incarcerated inmates should be provided educational information on the transmission, natural history, and medical management of HCV infection by appropriately trained personnel in accordance with BOP policy. The BOP peer-oriented video on infectious diseases, the attached information in **Appendix 2, Inmate Fact Sheet on Hepatitis B and C Viral Infection,** and other appropriate patient educational tools should be used to facilitate counseling efforts.

Screening method: The preferred screening test for HCV infection is an immunoassay (e.g., EIA or CIA) that measures antibodies to HCV antigens.

Non-sentenced inmates: Screening by immunoassay for HCV infection in asymptomatic, highly mobile, non-sentenced inmates should ordinarily not be pursued unless specifically indicated for medical reasons (e.g., symptomatic inmates, post-exposure management). Asymptomatic non-sentenced inmates in BOP detention facilities with histories of injection drug use or other high risk behaviors for HCV infection, should be counseled regarding their risk for HCV infection and behaviors that will reduce transmission of HCV infection to others during incarceration and upon release. Referrals to community HCV-testing sites should be made when appropriate.

Long-term inmates in BOP detention facilities should be screened for HCV infection in accordance with guidelines for sentenced inmates.

Sentenced inmates: An anti-HCV screening immunoassay, should be considered for the following sentenced inmates:

- Inmates who have injected illicit drugs;

- Inmates who have received a blood transfusion or organ transplant before 1992; or a clotting factor transfusion prior to 1987;

- Inmates on chronic hemodialysis (screen ALT levels monthly and for anti-HCV by immunoassay semiannually);

- Inmates who have received tattoos or body piercings while in jail or prison;

- Inmates with HIV infection or chronic HBV infection;

- Inmates with elevated ALT levels of unknown etiology;

- As clinically indicated, e.g., inmates with signs or symptoms of acute or chronic hepatitis and inmates with percutaneous exposures to blood.

NOTE: Sentenced inmates who have risk factors for HCV infection, but initially refuse testing, should be counseled periodically regarding the need for testing during routine patient encounters.

18. HEPATITIS C - CHRONIC HCV INFECTION (DIAGNOSIS/COUNSELING)

Diagnosis: The detection of anti-HCV by a screening immunoassay with a high signal-to-cutoff ratio, or in a person with risk factors for HCV infection strongly predicts HCV infection. Inmates with a positive anti-HCV screening immunoassay with a low signal-to-cutoff ratio, or inmates without risk factors for HCV infection (if no signal-to-cutoff ratio measured) should have a supplemental RIBA test.

An anti-HCV indeterminant result is reported when the screening immunoassay is positive but the supplemental RIBA is inconclusive, suggesting either resolving acute infection, chronic HCV infection, or a false-positive screening immunoassay. The correct diagnosis can usually be determined by obtaining a NAT for HCV RNA then 1 - 2 months later measuring anti-HCV by immunoassay and a NAT for HCV RNA.

The detection of anti-HCV does not differentiate between chronic HCV infection and resolved infection. Chronic infection is confirmed by detecting HCV RNA by a qualitative NAT for at least 6 months. HCV RNA detection is not ordinarily necessary at the time of initial diagnostic screening for inmates with risk factors for HCV infection or evidence of liver disease. However, HCV RNA detection by a qualitative NAT, with a lower limit of

detection of 50 IU/mL or less, is essential prior to initiating antiviral therapy.

NOTE: A single negative NAT for HCV RNA does not preclude chronic infection. The appropriate processing of NAT samples is also essential, since viral RNA is unstable and false negative tests may result from inadequate processing.

Patient counseling: Inmates diagnosed with chronic HCV infection should be counseled by a health care provider about the natural history of the infection, potential treatment options, and specific measures for preventing transmission of HCV infection to others (during incarceration and upon release), including the following information and recommendations:

- Most persons with chronic HCV infection will remain healthy, but a small number of persons will develop serious liver disease. Talk to your health care provider about your personal health status and risk of liver disease;

- Current drug treatment options for chronic hepatitis C are moderately effective. Newer medications should be available in the future that will improve treatment options. Medications may or may not be appropriate for you at this time. Talk to your doctor about your specific treatment plan;

- Do not shoot drugs, have sex with other inmates, or get a tattoo or body piercing while in prison;

- Do not share personal items that might have your blood on them, such as toothbrushes, dental appliances, nail-grooming equipment or razors;

- Cover cuts and skin sores to keep blood from contacting other persons;

- Before release, talk to a health care provider about specific ways you can reduce the risk of transmitting HCV infection to others after you are released;

- Upon release, markedly limit alcohol consumption or abstain altogether, and speak to a physician prior to taking any new medications, including over-the-counter medications such as nonsteroidal anti-inflammatory drugs (NSAIDS) and herbal remedies, that may damage your liver;

- Upon release, do not donate blood, body organs, other tissue or semen;

- Upon release, seek medical attention so that you receive

appropriate monitoring and treatment of your condition.

19. HEPATITIS C - CHRONIC HCV INFECTION (NATURAL HISTORY)

An estimated 50% - 85% of persons infected with HCV develop chronic infection, while 15% - 50% of newly infected persons are able to clear the virus spontaneously. Chronic HCV infection frequently results in high levels of HCV RNA in the blood, ranging from 10^5 to 10^7 international units (IU)/mL, despite the presence of HCV antibodies. The majority of persons with chronic HCV infection are asymptomatic.

Chronic HCV infection has an unpredictable course that is frequently characterized by fluctuations in ALT levels that may or may not be associated with significant liver disease. Approximately one-third of persons with chronic HCV infection have no evidence of liver disease.

An estimated 10% to 15% of persons with chronic HCV infection develop progressive fibrosis of the liver leading to cirrhosis. High levels of alcohol consumption, older age at the time of infection, HIV infection, chronic HBV infection, and male gender increase the risk of disease progression. The degree of viremia ("viral load") and the HCV genotype, however, do not affect the progression of liver disease. The degree of ALT elevation does not strongly correlate with the risk of disease progression, but persons who develop cirrhosis are more likely to have marked elevations in serum ALT levels.

Once cirrhosis develops in persons with chronic HCV infection, the risk of hepatocellular carcinoma (HCC) is approximately 1% to 4% per year. HCC is rare without underlying cirrhosis in persons with chronic HCV infection. Nonhepatic manifestations of HCV infection include cryoglobulinemia, glomerulonephritis, lymphoma, rheumatoid symptoms, and porphyria cutanea tarda. These clinical scenarios in inmates should prompt evaluation for chronic HCV infection.

20. HEPATITIS C - EVALUATION AND TREATMENT OF HCV INFECTIONS

Acute hepatitis C: Inmates diagnosed with acute hepatitis C should be considered for antiviral therapy in consultation with a physician with expertise in managing hepatitis. Reported data suggest that antiviral therapy is beneficial in treating persons with acute HCV infection, however, the timing and the optimal treatment regimen in this setting are uncertain; therefore treatment decisions should be made on a case-by-case basis.

Baseline evaluation (chronic HCV infection): A baseline

clinician evaluation should be conducted for all inmates diagnosed with HCV infection and include at least the following:

- Targeted history and physical examination to evaluate for signs and symptoms of liver disease, quantify prior alcohol consumption, determine risk behaviors for acquiring HCV infection, and estimate age of infection;

- Serum ALT, AST, bilirubin, alkaline phosphatase, albumin, prothrombin time, and further diagnostic evaluations as clinically warranted, for other potential causes of liver disease such as hemochromotosis, Wilson's disease, and autoimmune hepatitis;

- CBC with differential and platelet count;

- Renal function assessment (serum creatinine/BUN);

- Anti-HIV by immunoassay;

- HBsAg;

- Hepatitis B vaccination (Serologic prescreening for immunity to HBV infection should be considered for inmates who self-report previous, but undocumented hepatitis B vaccination by measuring anti-HBs; and for inmates from countries where HBV infection is endemic, e.g., Asia, the South Pacific, sub-Saharan Africa, and certain populations in the Arctic, South America, and the Middle East, by measuring total anti-HBc. Inmates with evidence of liver disease should be priority candidates for vaccination.);

- Hepatitis A vaccination (Serologic prescreening for immunity to HAV infection by testing for IgG (or total) anti-HAV should be considered for Native American inmates and foreign-born inmates from Latin America, Africa, Southeast Asia, and China where hepatitis A is endemic, and among inmates 50 years of age or older. Inmates with evidence of liver disease should be priority candidates for vaccination.)

Hepatocellular carcinoma (HCC) screening: Inmates with chronic HCV infection without cirrhosis are at low risk for HCC, therefore screening tests are not recommended for these patients. Inmates with chronic HCV infection and cirrhosis are at greater risk for HCC, but the optimal screening strategy for these patients is uncertain. Periodic screening for HCC, with a liver ultrasound (e.g. annually) and serum alpha-fetoprotein (e.g. every 6 months), should be considered for inmates with cirrhosis and HCV infection.

Periodic evaluations (chronic HCV infection): Inmates with chronic HCV infection should be monitored periodically in chronic care clinics. The frequency of monitoring should be based on patient-specific factors including candidacy for treatment, the degree of liver disease, and co-morbid conditions.

Assessing antiviral treatment contraindications: Inmates with chronic HCV infection who are potential candidates for antiviral therapy should first be assessed for treatment contraindications as listed in **Appendix 9, Contraindications to Interferon or Ribavirin Therapy** and in the drug manufacturers' information.

NOTE: Inmates with a history of psychiatric illness or with signs or symptoms of mental illness should be referred to a psychologist or psychiatrist for assessment. Inmates with serious mental illness should be treated and stabilized prior to pursuing a further work-up for treatment.

NOTE: Inmates with evidence of substance abuse, either in the present or the recent past (check urine toxicology screen if drug use is suspected and check Sentry for disciplinary actions related to drug or alcohol use.) should be referred for counseling and assessment prior to considering antiviral therapy.

Treatment considerations and evaluation strategy:

- **Detention center/short-term inmates**: Inmate candidates for hepatitis C treatment entering BOP short-term detention facilities should ordinarily not be started on antiviral therapy. Treatment decisions should be deferred until the inmate is sentenced and redesignated or released. Inmates entering BOP custody, who are already on treatment for hepatitis C, should be maintained on antiviral therapy, unless treatment must be discontinued for medical reasons. Consult with a Central Office physician if there are questions regarding continuation of therapy.

- **Long-term (sentenced) inmates**: Treating physicians should weigh the following factors in assessing the appropriateness of treatment and the best timing for initiating treatment as they counsel inmates with chronic HCV infection:

  - Only 10%-15% of persons with HCV infection develop significant long term complications of liver disease, usually 20-30 years after initial infection;

  - No laboratory parameters definitively predict which persons infected with HCV will develop cirrhosis or will respond to medical therapy;

- The presence of moderate to severe fibrosis and inflammation and necrosis on liver biopsy are currently the best markers for determining who should be offered antiviral therapy for hepatitis C;

- Antiviral therapy for hepatitis C is increasingly effective in clearing viremia and establishing sustained viral response rates (SVR);

- Although current antiviral therapy is usually well tolerated, serious drug side effects may occur;

- Future treatments for hepatitis C may be more effective and more easily tolerated.

An evidenced-based strategy for evaluating inmates for hepatitis C treatment is outlined in **Appendix 10 - Evaluation Strategy for Treatment of Hepatitis C.**

Identifying candidates for liver biopsy: Inmates with chronic HCV infection should be periodically evaluated and have ALT levels monitored to help determine if liver biopsy is warranted in accordance with the following:

- **Normal ALT**: Approximately 30% of persons with chronic HCV infection have normal ALT levels. Inmates with normal ALT levels should have ALT levels remeasured several times over the next 2 to 12 months. Inmates with persistently normal ALT levels (at least 3 normal values over a 6 to 12 month period) with no clinical or laboratory evidence of liver disease, are unlikely to have marked liver inflammation or fibrosis.

NOTE: Inmates with persistently normal ALT levels may have resolved HCV infection; therefore a NAT for HCV RNA should be obtained to confirm chronic HCV infection; or if negative, should be repeated to confirm resolved HCV infection.

A liver biopsy is usually not warranted if ALT levels are persistently normal. A targeted history and physical examination should be conducted every 6 to 12 months along with platelet count, AST, ALT, alkaline phosphatase and prothrombin time measurements. A decreased platelet count, an increased AST/ALT (e.g., ratio > 1), a decreasing serum albumin, an increased alkaline phosphatase, or a prolonged prothrombin time may indicate underlying liver disease and warrant further evaluation. Inmates with HIV infection and HCV infection with persistently normal ALT levels may be candidates for liver biopsy on a case by case basis, e.g., need to establish absence or presence of liver disease and need for hepatitis C treatment, in patient who may